urea). Specific individual parameters that determine the dose of HD and HF were dictated by the study protocol, but others were prescribed individually (Appendices 1 and 2 in the article) with respect to temporary individual patient clinical characteristics and treatment goals.

We agree with many other authors that the issues of dialysis dose and of the adequacy parameters are much more complex and should be considered more extensively than just in terms of removal of small solutes (e.g. urea clearance or surrogate markers), which alone cannot fully reflect dialysis efficiency, nor cover the wide-ranging goals of dialysis treatment, especially not in critically ill patients with AKI as part of multi-organ failure (MOF).

Same as in our everyday clinical practice, dialysis parameters determining the dose were not prescribed on the basis of single particular marker solely, but taking into consideration all the main problems in AKI that can and should be controlled by dialysis support (i.e. uraemic retention, fluid overload, electrolyte and acid–base disequilibrium). Except for mean daily urea and creatinine concentration, all these measurements and ‘markers of adequate dialysis’ were not analysed. Even so, we believe that according to our clinical practice, the most important aspects of dialysis support were managed adequately, efficiently and in compliance with the current recommendations.

In critically ill patients with AKI, there is presently no consensus on the optimal dialysis dose. Many recent studies proved that in this specific group of patients, more intensive (high-dose) dialysis treatment does not improve the clinical outcomes or provide any additional clinical benefit when compared with the conventional, less-intensive (standard-dose) treatment strategy, regardless of dialysis modality [2–6].

Concerning the frequency/schedule of dialysis procedures, they were certainly prescribed daily whenever necessary (e.g. in anuric and hypervolaemic patients, in haemodynamically unstable patients with low neto ultrafiltration possible, etc.). We strongly agree with the comment that an individual approach to selection of all characteristics of dialysis care is needed.

Pre-treatment values of urea and creatinine in our study indeed suggest that, in our clinical practice, initiation of renal replacement therapy is quite ‘late’ when compared with other studies/practices [3, 4]. However, except for emergency indications, clinical and biochemical parameters pointing to the optimal time to initiate dialysis support in critically ill patients with AKI as part of MOF remain undefined. Moreover, studies did not show better patient outcomes with ‘early’ versus ‘late’ dialysis initiation [2, 7, 8]. On the contrary, in a study by Bagshaw et al. [7], late initiation (when stratified by median creatinine at the time renal replacement therapy was started) was associated with lower mortality.

As a final note, there is currently no evidence that, in critically ill patients with AKI, any particular dialysis modality is superior to others owing to better clinical outcomes. We have demonstrated that, in the hands of experienced practitioners, both HD and HF can be performed safely and effectively also in the most severely ill patients. We believe that individual dialysis treatment, including individual selection of dialysis modality as well as all other dialysis parameters, is the optimal approach to dialysis management of AKI in critically ill patients with MOF that could potentially improve the grave prognosis of these patients.

Conflict of interest statement. None declared.

Department of Renal Nephrology, University Medical Centre Ljubljana, Jadranka Buturović-Ponikvar, Rafael Ponikvar Ljubljana, Slovenia
Correspondence and offprint requests to: Nataša Škofic; E-mail: natasa.skofic@mf.uni-lj.si


doi: 10.1093/ndt/gfs311

The search for perfect biomarkers in acute kidney damage: the case of NGAL, from AKI to acute pyelonephritis: back to the clinic?

Sir,

The paper by Schinstock et al. [1] regards one of the most promising biomarkers introduced into clinical practice, the versatile neutrophil gelatinase-associated lipocandin (NGAL). We are all looking for the perfect biomarker of kidney damage: rapidly tested, allowing a fast, objective and reliable selection of patients at risk for acute complications and needing hospitalization or intensive care. The

"The search for perfect biomarkers in acute kidney damage: the case of NGAL, from AKI to acute pyelonephritis: back to the clinic?"
paper by Schinstock et al., addressing the risk of developing acute kidney injury (AKI) during hospitalization, reports a significant increase of NGAL paralleling the development and severity of AKI. Statistical significance is not always synonymous with clinical relevance and, in spite of statistically significant differences, the sensitivity and specificity for NGAL in the prediction of AKI are relatively low (65%). Indeed the authors comment that the high dispersion of data underlines the need for further stratification [1].

We would like to briefly mention our experience with urinary NGAL in a different context, acute pyelonephritis (APN) and upper urinary tract infections (UTIs), leading to similar promises and uncertainties. AKI and APN share the presence of acute, mainly tubulointerstitial kidney injury, diffuse in AKI and limited to a section of the kidney parenchyma in APN. The potential relevance of a marker of kidney damage in UTI is high since the presence of parenchymal lesions requires longer antibiotic therapy, as recently reported by Rollino et al. [2, 3]. Clinical and laboratory data allow a diagnosis of upper UTI but are unable to identify parenchymal involvement from ‘pyelitis’. Second-line, expensive and often not readily available imaging techniques, such as computerized tomography or magnetic resonance (MR), are needed for the definition of APN [2, 3].

A few studies have suggested that NGAL could discriminate the severity of infection in children, in kidney grafts and in a mouse model [4–6]. Therefore, in January–December 2011, we obtained a urine sample for NGAL in 50 patients (46 females and 4 males) hospitalized in our setting who underwent MR within 1 week from hospitalization for clinical suspicion of APN. NGAL was tested by a commercially available kit (Architect NGAL chemiluminescent immunoassay, CMIA), according to the manufacturer’s instructions.

MR indicated pyelonephritis in 38 cases and was negative in 12 (diagnoses: 9 upper UTIs, without kidney involvement, 1 infected kidney cyst, 1 prostatitis, 1 diverticulitis). APN was primary or non-complicated in 29 cases, secondary to anatomo-functional predisposing factors in 9. A further sample for NGAL was collected 3–6 weeks from admission at a second MR in 24 patients affected by APN (18 negative, 6 positive). Analysing all cases with positive and negative MR throughout the follow-up, median NGAL was 74 ng/mL (4.9–348.2) in positive MR and 53.2 ng/mL (1.3–210.3) in negative MR. To avoid the bias of pre-existing renal damage, we also limited the analysis to primary APN: median NGAL was 74 ng/mL (4.9–314.2) in APN and 34.8 ng/mL (9.6–210.3) in negative cases. Due to the low numbers and high dispersion, the differences do not reach statistical significance (P = 0.102 and 0.108, respectively). While no correlation with urinalysis was found, possibly because MR was performed after 2–5 days of hospitalization and antibiotic therapy, a qualitative analysis of the outliers suggested interference by nephrotoxic antibiotics, a hypothesis to be tested on a larger scale.

Interestingly, the wide range of data and the median NGAL in our smaller group of ‘non-APN’ patients (34.8 ng/mL; 9.6–210.3) can be considered equivalent to what was recorded in the larger population of patients without AKI (23.0 ng/mL; 0.0–2717.0) [1].

One might wonder, in the face of such disperse data, if we really need a further test or if the lesson from the search for ‘perfect biomarkers’ should lead us to reconsider simpler approaches, such as microscopic urinalysis in AKI and a careful clinical and drug history in APN, as tools to be re-developed in an era of economic crisis.

Conflict of interest statement. None declared.

1ASOU San Luigi Gonzaga, Nefrologia, Scienze Mediche Biologiche, Orbassano, Torino, Italy
2ASOU San Luigi Gonzaga, Laboratorio, Scienze Mediche Biologiche, Orbassano, Torino, Italy
3ASOU San Luigi Gonzaga, Radiologia, Scienze Cliniche Biologiche, Orbassano, Torino, Italy
Correspondence and offprint requests to: Giorgina Barbara Piccoli; E-mail: gbpiccoli@yahoo.it


doi: 10.1093/ndt/gfs331